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August 15, 2003

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Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Art Unit 2654

Re: U.S. Utility Continuation Patent Application
Appl. No. 09/848,353; Filed: May 4, 2001
For: **Modulating the Permeability of a Physiological Barrier with an Agent that Modulates Tyrosine Phosphorylation (As Amended)**
Inventor: Staddon et al.
Our Ref: 0623.0410001/LBB/BJD

Sir:

Transmitted herewith for appropriate action are the following documents:

1. First Supplemental Information Disclosure Statement (IDS);

2. A listing of the cited documents on Form PTO-1449 (7 pages);

3. Copies of the twenty four (24) documents listed on the Form PTO-1449 **(AB1-AC1, AN1-AP1, and AR20-AR26)**; and

4. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Brian J. Del Buono
Attorney for Applicants
Registration No. 42,473

LBB/BJD/JKM/adw
Enclosures

SKGF_DC1:168314.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Staddon *et al.*

Appl. No. 09/848,353

Filed: May 4, 2001

For: **Modulating the Permeability of a Physiological Barrier with an Agent that Modulates Tyrosine Phosphorylation (As Amended)**

Confirmation No. 1015

Art Unit: 1631

Examiner: Borin, M.L.

Atty. Docket: 0623.04100/DVE/BB/BJD/JKM

First Supplemental Information Disclosure Statement

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. The numbering on this First Supplemental Information Disclosure Statement is a continuation of the numbering in Applicants' Information Disclosure Statement filed October 31, 2001, in connection with the above-captioned application. A copy of each document is also provided.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates

should not be construed as an admission that the information was actually published on the date indicated.

This First Supplemental Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered. This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist.

Consideration of the cited documents and making the same of record in the prosecution of the above-identified application is respectfully requested. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Brian J. Del Buono
Attorney for Applicants
Registration No. 42,473

Date: Aug. 15 2003

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FORM PTO-1449

FIRST SUPPLEMENTAL
INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.	APPLICATION NO
0623.0410001/LBB/BJD/JKM	09/848,778
APPLICANT: Staddon *et al.*	
FILING DATE: May 4, 2001	GROUP: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB1	6,245,888 B1	06/12/2001	Staddon			05/19/1997
	AC1	6,312,686 B1	11/06/2001	Staddon *et al.*			12/23/1997
	AD						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN1	WO 95/13820	05/26/1995	WIPO			Yes No
	AO1	WO 96/16170	05/30/1996	WIPO			Yes No
	AP1	WO 98/14186	04/09/1998	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	20	Aberle, H., *et al.*, "Cadherin-Catenin Complex: Protein Interactions and Their Implications for Cadherin Function," *J. Cell. Biochem.* 61:514-523, Wiley-Liss, Inc. (1996).
	AS	20	Balda, M.S., *et al.*, "Assembly of the Tight Junction: The Role of Diacylglycerol," *J. Cell Biol.* 123:293-302, The Rockefeller University Press (October 1993).
	AT	20	Breier, G , *et al.*, "Angiogenesis in Embryos and Ischemic Diseases," *Thromb. Haemost.* 78:678-683, F.K. Schattauer Verlagsgesellschaft (1997).

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

FIRST SUPPLEMENTAL
INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.	APPLICATION NO.
0623.0410001/LBB/BJD/JKM	09/848,353
APPLICANT: Staddon *et al.*	
FILING DATE: May 4, 2001	GROUP: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	21	Daniel, J.M., and Reynolds, A.B., "Tyrosine phosphorylation and cadherin/catenin function," *BioEssays 19*:883-891, The Company of Biologists Limited (1997).
	AS	21	Esser, S., *et al.*, "Vascular endothelial growth factor induces VE-cadherin tyrosine phosphorylation in endothelial cells," *J. Cell Sci. 111*:1853-1865, The Company of Biologists Limited (1998).
	AT	21	Ferrara, N., and Davis-Smyth, T., "The Biology of Vascular Endothelial Growth Factor," *Endocrine Rev. 18*:4-25, The Endocrine Society (1997).

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FORM PTO-1449

FIRST SUPPLEMENTAL
INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.	APPLICATION NO.
0623.0410001/LBB/BJD/JKM	09/848,359
APPLICANT: Staddon *et al.*	
FILING DATE: May 4, 2001	GROUP: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	22	Fong, T.A.T., *et al.*, "SU5416 Is a Potent and Selective Inhibitor of the Vascular Endothelial Growth Factor Receptor (Flk-1/KDR) That Inhibits Tyrosine Kinase Catalysis, Tumor Vascularization, and Growth of Multiple Tumor Types," *Cancer Res.* 59:99-106, The American Association for Cancer Research (1999).
	AS	22	Gumbiner, B.M., "Cell Adhesion: The Molecular Basis of Tissue Architecture and Morphogenesis," *Cell* 84:345-357, Cell Press (1996).
	AT	22	Herrenknecht, K., *et al.*, "Tyrosine Phosphorylation and Tight Junction Permeability. II," Abstract (distributed at meeting) from Autmn meeting of the British Society for Cell Biology, University of Oxford, UK, Semptember 18-21, 1994.

EXAMINER	DATE CONSIDERED

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FORM PTO-1449 FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0623.0410001/LBB/BJD/JKM	APPLICATION NO. 09/848,35[illegible]
	APPLICANT Staddon *et al.*	
	FILING DATE May 4, 2001	GROUP 1631

U.S. PATENT DOCUMENTS

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	AA						
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	23	Jones, A., and Harris, A.L., "New Developments in Angiogenesis: A Major Mechanism for Tumor Growth and Target for Therapy," *Cancer J.* 4:209-217, Scientific American (1998).
	AS	23	Neufeld, G., *et al.*, "Similarities and differences between the vascular endothelial growth factor (VEGF) splice variants," *Cancer Metastasis Rev.* 15:153-158, Kluwer Academic Publishers (1996).
	AT	23	Ratcliffe, M.J., *et al.*, "Dephosphorylation of the Cadherin-associated p100/p120 Proteins in Response to Activation of Protein Kinase C in Epithelial Cells," *J. Biol. Chem.* 272:31894-31901, The American Society for Biochemistry and Molecular Biology, Inc. (1997).

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	24	Ratcliffe, M.J., *et al.*, "Dephosphorylation of the catenins p120 and p100 in endothelial cells in response to inflammatory stimuli," *Biochem. J. 338*:471-478, Biochemical Society (1999).
	AS	24	Soler, A.P., *et al.*, "Tissue remodeling during tumor necrosis factor-induced apoptosis in LLC-PK$_1$ renal epithelial cells," *Am. J. Physiol. 270*:F869-F879, American Physiological Society (1996).
	AT	24	Staddon, J.M., *et al.*, "p120, a p120-Related Protein (p100), and the Cadherin/Catenin Complex," *J. Cell Biol. 130*:369-381, The Rockefeller University Press (1995).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	25	Sun, L., *et al.*, "Synthesis and Biological Evaluations of 3-Substituted Indolin-2-ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular Receptor Tyrosine Kinases," *J. Med. Chem.* *41*:2588-2603, American Chemical Society (1998).
	AS	25	Uehara, Y., *et al.*, "Irreversible Inhibition of V-src Tyrosine Kinase Activity by Herbimycin A and its Abrogation by Sulfhydryl Compounds," *Biochem. Biophys. Res. Commun.* *163*:803-809, Academic Press (1989).
	AT	25	Vermeulen, S., *et al.*, "Regulation of the Invasion Suppressor Function of the Cadherin/Catenin Complex," *Path. Res. Pract.* *192*:694-707, Gustav Fischer Verlag (1996).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	26	Wong, E.Y.M., *et al.*, "Vascular endothelial growth factor stimulates desphosphorylation of the catenins p120 and p100 in endothelial cells," *Biochem. J.* 346:209-216, Biochemical Society (2000).
	AS		
	AT		

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